

The 35 USC §101 Rejection:

Claim 1 stands rejected provisionally under 35 U.S.C. §101 for double patenting in light of claim 1 of copending Application No. 08/980,394. Applicants intend to cancel claim 1 in the co-pending application so as to render this rejection moot.

The 35 USC §112(1) Rejection:

Claim 2 is rejected under 35 USC §112, first paragraph as being non-enabled. This rejection is respectfully traversed.

The Examiner states that "The specification fails to teach an antibody that specific (sic) to the chloride channel protein. The specification fails to teach how to obtain a chloride channel protein that is specific to glial-derived or meningioma-derived tumor cells and to make an antibody against it." Applicants disagree.

On pages 56 and 57, in Example 24, "Molecular Identity of GCC", Applicants teach how to obtain a chloride channel protein against which an antibody may be made. Example 24 details how a protein of about 70 kDa is isolated from glioma membranes for use in affinity purification. This purified protein can be used to generate antibodies. Antibody preparation from purified proteins is routine in this art. The Examiner has not produced any evidence that a person

having ordinary skill in this art would not be able to produce an antibody against the chloride channel protein specific to glial-derived or meningioma-derived tumor cells disclosed by the instant application.

Claims 1-4 are rejected under 35 USC §112, first paragraph as being non-enabled. This rejection is respectfully traversed.

Regarding dosage, given the well-established nature of the glioma-specific chloride channel, as supported by the specification (see, e.g., page 4, line 7-page 5, line 25; Figures 2, 4-11, 13-20; page 13, line 10-page 14, line 24), it would not require undue experimentation on the part of one with ordinary skill in the art to determine a dosage range for the composition of the instant invention. One must typically perform a series of dosages when employing any new antibody in routine laboratory use, to optimize the dosage for the particular application.

The issue of what constitutes "undue" experimentation has been extensively discussed (see, e.g., *In re Wands*, 858 F.2d at 737; *In re Forman*, 230 USPQ at 547). In *In re Wands*, the court writes: "Enablement is not precluded by the necessity for some experimentation such as routine screening." (*Id.* at 736-737).

With respect to route of administration, there is no data that the Applicants' composition would not be cross the blood-brain barrier. Regardless, Applicants' composition could be administered at the time of surgery into the tumor itself. Applicants' need not teach multiple routes of administration.

Examiner further argues that the *in vitro* assays reported do not adequately represent potential for treatment of a primary tumor. Applicants disagree. Findings from cell lines were extended in the instant invention by work from patient biopsies. Clearly, Applicants have presented ample evidence that a glioma-specific receptor has been found and can be targeted therapeutically. Xenograft data in which human tumor cells grow tumors in mice also supports the contention that this is a glioma-specific receptor: the tumor cells express this protein, whereas the host cells do not. For these reasons, Applicants submit that claims 1-4 are enabled and request that the rejection under 35 USC §112 be withdrawn.

The 35 USC §112(2) Rejection

Claims 3 and 4 stand rejected under 35 USC §112, second paragraph as being indefinite. This rejection is respectfully traversed.

The Examiner contends that the term "chlorotoxin-like protein" lacks metes and bounds. Applicants direct Examiner to page 14 of the Specification, where, on lines 1-2, chlorotoxin-like proteins are identified as "(fusion proteins)". As is well known in the art, a fusion protein may contain a protein of interest as a targeting moiety, in this case chlorotoxin, fused with a cytotoxic moiety. Examples of such cytotoxic moieties are ricin, saporin and *Pseudomonas* exotoxin. Thus, Applicants respectfully request that the rejection of claims 3 and 4 under 35 U.S.C §112, second paragraph be withdrawn.

The 35 USC §102 Rejection

Claims 1 and 3 stand rejected under 35 USC §102(a) as being anticipated by **Ullrich** et al. (1996). This rejection is traversed.

The instant application is a divisional application claiming priority of the parent application, U.S. Serial Number 08/744,154, which in turn claims priority of provisional application 60/009,283, filed December 27, 1995. Thus, **Ullrich** et al. (1996) is not an effective reference under 35 USC §102(a).

Claim 1 is further rejected under 35 USC §102(b) as being anticipated by **Phillips** et al. (1994). This rejection is traversed.

Claim 1 has been amended to more specifically point out and claim the Applicants' invention. Therefore, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C §102 be withdrawn.

The 35 USC §103 Rejection:

Claims 1 and 3-4 are rejected under 35 USC §103(a) as being unpatentable over **DeBin** et al. (1993) or **Malinowska** et al. (1994) in view of **Ullrich** et al. (1996). This rejection is traversed.

As discussed above, **Ullrich** et al. is not an effective reference. Neither **DeBin** et al. (1993) nor **Malinowska** et al. describe, teach or suggest a pharmaceutical composition, comprising a ligand which binds specifically to glial-derived or meningioma-derived tumor cells and a pharmaceutically acceptable carrier, wherein the ligand is an antibody which recognizes an antigen that is a glioma or meningioma specific chloride channel or a chlorotoxin-like compound. Accordingly, Applicants respectfully request that the rejection of claims 1 and 4 under 35 USC §103(a) be withdrawn.

This is intended to be a complete response to the Office Action mailed August 5, 1998. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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